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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,788	YU ET AL.	
	Examin r	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *25-48 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1) Claims 1 to 50 are pending in the instant application.

2) Claims 25 to 48 and 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the correspondence filed 02 September of 2003. The traversal is on the ground(s) that a search of the different inventions in a single application would pose no undue burden. This is not found persuasive because M.P.E.P. 803 states that:

> " For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant."

Serious burden was shown in the original requirement by the separate classification and separate status in the art of the different inventions. Applicant has provided neither a showing nor evidence to the contrary.

The requirement is still deemed proper and is therefore made FINAL.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3) Claims 1 to 24 and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and how to use requirements. These claims encompass subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

The instant specification provides a precise written description of isolated nucleic acid encoding two very specific, naturally occurring human calcium sensing receptor isoform polypeptides identified therein as CaSRc and CaSRd, and the proteins encoded thereby. The instant specification discloses that CaSRc corresponds to an isoform of a previously described human calcium sensing receptor represented by the amino acid sequence of SEQ ID NO:12 and differing therefrom by the absence of amino acid residues 460 to 536 from that sequence. It further discloses that CaSRd corresponds to another isoform of that previously described human calcium sensing receptor and differs therefrom by the absence of amino acids 358 to 462 from of SEQ ID NO:12. The instant claims, however, encompass an isolated nucleic acid encoding any isoform of a human calcium sensing receptor in which "about" 231 nucleotides have been deleted from that nucleic acid or "about 77" amino acids have deleted from the receptor and "allelic variants thereof". An artisan of ordinary skill in the art of molecular biology would not reasonably believe that each of the vast majority of structural embodiments encompassed by the limitation "having about 77 amino acids deleted from SEQ ID NO12" would correspond to an isoform of a human calcium sensing receptor. Whereas the instant claims encompass nucleic acids encoding potentially thousands of structural embodiments of the claimed invention, the instant specification only describes two "human" "isoforms:, and one of ordinary skill would not believe that those two embodiments constitute a representative number of species within the claimed genus of

nucleic acids or polypeptides encoded thereby. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of two isolated DNAs encoding two particular, naturally occurring human calcium sensing receptor isoform polypeptides having very specific physical and structural properties, the instant specification does not provide a structural formula which is definitive of all naturally

occurring human calcium sensing receptor isoform polypeptides or of allelic variants of either of those two proteins particular proteins described therein. Whereas the instant specification may identify some properties that are common to the two receptors that are disclosed in the instant specification, it does not identify those defining structural elements that provide the functional and structural properties of all naturally occurring human calcium sensing receptor isoform polypeptides.

Further, the two proteins identified in the instant specification as CaSRc and CaSRd are useful only in so far as they behave in a manner that is predictive of a naturally occurring protein. As such, they are useful in the identification of compounds that influence calcium regulation within the kidney. Whereas one could readily delete "about 77 amino acids" from any portion of SEQ ID NO12 to produce a protein meeting the structural limitations of the claims, one would not have a reasonable expectation that the resultant protein would function in an authentic manner and the instant specification does not disclose how to use a calcium sensing receptor isoform that does not function in an authentic manner. For example, there is no evidence of record that the specific embodiment encompassed by claims 5 and 23 corresponds to a naturally occurring receptor or that it functions in an authentic manner which would provide a specific and substantial utility to the public in the recited form.

In so far as one could repeat the techniques of Applicant and obtain an isolated nucleic acid encoding a human calcium sensing receptor isoform of the instant

invention, one does not have a reasonable expectation that such efforts would yield an isolated nucleic acid encoding anything other than the two isoforms already obtained. There is no evidence of record that other such isoforms exist or a description of how they differ structurally and/or functionally from those two specific isoforms that were discovered by Applicant. *Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd.*, 18 U.S.P.Q. 2d, 1016 (Fed. Cir. 1991), held that;

> "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and describe how to obtain it. *See Oka,* 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.,* encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.,* until after the gene has been isolated".

Claim 49 is defined by function alone and, therefore, constitutes nothing more that a single means claim. A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. In re Hyatt , 708 F.2d 712,>714 - 715,< 218 USPQ 195>, 197< (Fed. Cir. 1983) (A single means claim which covered every conceivable means for achieving the stated purpose was held

nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor.). When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. Claim 49 essentially constitutes nothing more than a wish to know the identity of any polypeptide having the recited activity. See M.P.E.P. 2164.08(a)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4) Claims 1 to 24 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4.1) Claims 1 to 24 are vague and indefinite in their recitation of the limitation "about" in reference to nucleotides and amino acids. For example, claims 1 and 19 are vague because the metes and bounds of limitations such as "about 231 nucleotides" and "about 77 amino acids are undeterminable. Even though the use of the term "about" in a claim is inherently vague and indefinite, its use is appropriate when employed to limit a value which is composed of infinitely divisible units such as inches, meters, grams and pints where it is impractical to produce an item which has exactly the dimension recited. Even if one could practically produce an item which is exactly 1 inch in length, the length of that item is conditional upon the temperature at which it is measured. However, when defining an invention in terms of indivisible numerical units

such as the number of nucleotides in a nucleic acid, the number of amino acids in a polypeptide or the number of legs on a chair or table, the term "about" is unacceptably vague and indefinite since it is practical to employ a term which possesses the required precision. If, for example, it is Applicants' intent that the claims should encompass a polypeptide comprising at least 970 amino acids but no more that 1010 amino acids then this is exactly what the claim should recite. Whereas one would reasonably interpret the term "about one inch" as encompassing any value from 0.90 inches to 1.10 inches one would not know if a term such as "about 77 amino acids" would include or exclude 75, 80, or even 65 amino acids. Claim 5 is particularly confusing in this respect because it depends from claim 1 and recites a deletion of over 500 nucleotides, which would not appear to be "about 231" as recited in claim 1.

4.2) Claim 1 is confusing because it refers to "a deletion of about 231 nucleotides when compared to the wild-type form of receptor as depicted in SEQ ID NO:11". This text should probably refer to "231 nucleotides when compared to the nucleic acid encoding the wild-type form of receptor as depicted in SEQ ID NO:11". This is particularly true in view of the fact that SEQ ID NO:11 is a nucleotide sequence and not an amino acid sequence. Claims 2 to 18 are vague and indefinite in so far as they depend from claim 1 for this element.

4.3) Claims 2 and 20 are vague and indefinite because there is no antecedent basis for "the extracellular domain of the receptor". It is old and well known in the art that a calcium sensing receptor of the instant invention is a member of the G protein-coupled receptor family. It is also well known in the art that the defining structural

features of all G protein-coupled receptors include four extracellular domains. This claim should probably refer to "the first extracellular domain of the receptor". Claims 3 to 5, 7, 8 and 20 to 23 are vague and indefinite in so far as they depend from either of claims 2 or 20 for this element.

4.4) Claim 6 is vague and indefinite because the limitation "under stringent conditions" is conditional and no single set of defining conditions is recited in the claim or the specification. In fact, this term may not even appear in the specification. Further, those hybridization conditions described on pages 7 and 8 of the specification are expressly identified therein as exemplary ("*e.g.*").

4.5) Claim 49 is vague and indefinite in so far as it refers to "the wild-type CaSR" because there is no single protein recognized in the art as "the wild-type" calcium sensing receptor. Applicant is advised that the two proteins identified in the instant specification as CaSRc and CaSRd are "wild-type" proteins because they are naturally occurring. The term "wild-type" encompasses any genotype or phenotype that occurs in nature and does not generally refer to one phenotype. For example, a "wild-type" hair color for humans can include black, brown, blond, red, white and gray. The facts presented in the instant application support a conclusion that CaSR, CaSRc and CaSRd are all naturally occurring products of the same gene and arise through different mRNA splicing. Therefore, they all correspond to a "wild-type" form of CaSR.

5) The art of record did not disclose or suggest an isolated nucleic acid encoding SEQ ID NO:8 or 10 of the instant application or an isolated protein comprising either of those sequences.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1600